Published in final edited form as:

Urology. 2017 August ; 106: 26–31. doi:10.1016/j.urology.2017.03.058.

Overactive bladder is strongly associated with frailty in older individuals

Anne M. Suskind, MD, MS[1], **Kathryn Quanstrom**[1], **Shoujun Zhao, PhD**, **Mark Bridge**[1], **Louise C. Walter, MD**[2,3], **John Neuhaus, PhD**[4], and **Emily Finlayson, MD, MS**[5]

[1]University of California, San Francisco Department of Urology

[2]University of California, San Francisco, Division of Geriatrics

[3]Veterans Affairs Medical Center, San Francisco, California, Division of Geriatrics

[4]University of California, San Francisco, Department of Epidemiology and Biostatistics

[5]University of California, San Francisco, Department of Surgery

Abstract

Objectives—To understand the relationship between age, frailty and overactive bladder (OAB).

Methods—This is a prospective study of individuals age ≥65 presenting to an academic urology practice between December 2015 and July 2016. All patients had a Timed Up and Go Test (TUGT), a parsimonious measure of frailty, on intake and were thereby categorized as fast (≤10 sec), intermediate (11-14 sec) and slow (≥15 sec). The TUGT and other clinical data were abstracted from the electronic medical record (EMR) using direct queries. Logistic regression was used to examine the relationship between frailty and the diagnosis of OAB, adjusting for age, gender and race.

Results—Our cohort included 201 and 1162 individuals with and without OAB, respectively. Individuals with OAB had slower TUGTs (13.7 ± 7.9 sec) than their non-OAB counterparts (10.9 ± 5.2 sec), $p<0.0001$, with 32.3% and 11.0% of OAB and non-OAB individuals being categorized as slow, or frail. In multivariable analysis, slower TUGT was a significant predictor of OAB (adjusted OR 3.0; 95% CI 2.0-4.8). Age was not independently associated with this diagnosis (p values >0.05 for each age group).

Conclusions—Patients with OAB are statistically significantly frailer than individuals seeking care for other non-oncologic urologic diagnoses. Frailty, when adjusted for age, race and gender, is a statistically significant predictor of OAB. Furthermore, frailty should be considered when caring for older patients with OAB and OAB should be assessed when caring for frail older patients.

Keywords

OAB; timed up and go test; TUGT; geriatric; lower urinary tract; elderly

Corresponding Author: Anne M Suskind, MD, MS, 400 Parnassus Ave, Box 0738, San Francisco, CA 94143, 415-476-1611, Fax: 415-476-8849, Anne.Suskind@ucsf.edu.

Introduction

Overactive bladder affects approximately one third of men and women over the age of 65.[1,2] Defined as urgency (with or without leakage of urine) and usually associated with increased frequency and nocturia,[3] overactive bladder is associated with increased mortality,[4] morbidity,[5] marked decrease in health-related quality of life[6] and significant economic burdens totaling over $65 billion per year.[7]

Current paradigms suggest that the pathophysiology associated with aging is responsible for the development of symptoms of overactive bladder. These changes include, but are not limited to, decreased bladder capacity, decreased bladder sensation, impaired detrusor contractile function during voiding and increased residual volume[8,9] However, increasing age is also associated with increasing frailty, defined as a multifactorial syndrome manifested by a reduction in physiologic reserve and in the ability to resist stressors.[10] This brings to question whether it is really age, or rather, frailty that impacts the presence of overactive bladder.

Using data from the University of California, San Francisco Geriatric Urology Database (UCSF-GUD) on all individuals ages 65 and older visiting our academic non-oncologic urology clinical practice, we evaluated the association between frailty, measured by the Timed Up and Go Test (TUGT), and a diagnosis of overactive bladder. Findings from this study will help to unravel the complicated relationship between age, frailty and overactive bladder to help further our understanding of this common and problematic condition in the older population and potentially lay the groundwork for a new conceptual model of overactive bladder.

Materials and Methods

Patients and Database

We used data from the UCSF-GUD from December 2015 to July 2016. This Institutional Review Board (IRB) approved database prospectively collects data on all patients age 65 and older presenting to our adult non-oncologic urology clinical practice. Data are regularly extracted directly from the electronic medical record (EPIC) using extract, transform and load (ETL) routines via the clinical data reporting database (Clarity) and datamart (Cogito).

Specifically, data extraction occurred in 6 steps. The first step started with a query that identified patients with a completed appointment in a particular clinic with a relevant list of providers. The second step took the set of patients identified in the first step and calculated their age in years (to ensure that they were 65 years or older at the time of the visit) and obtained relevant demographic information. Third, we ran queries for all TUGT values entered into EPIC in the specified appointment date range and crosschecked this output with that from step 2 to ensure that there were no missed values. Fourth, we abstracted operating room data and current procedural terminology (CPT) codes that were scheduled with the relevant list of providers during the time range of the study. Procedures annotated as “cancelled” were eliminated and the remainder of the procedures were connected with the patients identified in step 2. Fifth, we abstracted all problem list data from the patients

identified in step 2 including International Statistical Classification of Diseases (ICD-9 and 10) codes, diagnosis name entered into the chart, diagnosis group, noted date, problem status and resolved date where appropriate. Finally, we abstracted medication data for patients identified in stage 2 including the pharmacologic and therapeutic medication classes.

Outcome

We identified patients in the UCSF-GUD with a diagnosis of overactive bladder using the followingICD-9 and 10 codes: 596.51 hypertonicity of bladder; 788.63 urgency of urination; 788.41 urinary frequency; 788.31 urge incontinence; 788.33 mixed incontinence. We originally identified 226 individuals with overactive bladder based on coding alone. We then reviewed each of the charts on individuals with an overactive bladder diagnosis and found that 25 of these charts represented patients who had other types of lower urinary tract symptoms, for an overall accuracy of 89%. We excluded these 25 patients with other diagnoses from our analyses so that 100% of our cohort had a diagnosis of overactive bladder. Seventy-four percent of individuals had their diagnosis of overactive bladder on the same date as their TUGT. Patients were excluded from the cohort if they declined the TUGT, if no TUGT was recorded, or if they were in a wheelchair, precluding them from being able to perform the TUGT.

Covariates

We used the TUGT as our measure of frailty, which we administer to all patients age 65 and older upon intake to our clinical practice at each office visit upon their approval. In order to complete this test, individuals are instructed to stand up from a chair, walk 10 feet at a normal pace (they can use a walker, cane, or other walking device if needed), walk back to the chair and sit down again. This task requires assimilation of several elements including understanding and following directions, transfer from a seated to a standing position (and vice versa), walking speed, strength and balance. Slower walking speed has demonstrated sensitivity and specificity as a measure of frailty,[11] and has been associated with increased postoperative complications across surgical subspecialties. The TUGT can be used to categorize individuals as “fast” (≤10 seconds), “intermediate” (11-14 seconds) and “slow” (≥15 seconds), with corresponding implications for frailty being “not frail”, “intermediately frail” and “frail”, respectively.[12] Individuals in wheelchairs are not able to complete this test, and are noted as such in the database. If an individual had more than one office visit within the study period, only their first recorded TUGT was used in the analyses. The TUGT values in addition to demographic and clinical information pertaining to age (age groups: 65-70, 71-75, 75-80, 81+), sex, race (White, Black, Asian, other), number of medications (medication groups: 1-5, 6-10, 11-15, 16-20, >20), the presence of urinary incontinence [based on ICD-9 codes 788.31 (urge incontinence) and 788.32 (stress incontinence male or female)] and number of office visits were abstracted from the database.

Statistical Analysis

Summary characteristics of patients with and without a diagnosis of overactive bladder were presented as averages with standard deviations or as numbers and percentages and were compared using t-tests with two-sided p values <0.05. A multivariable logistic regression analysis was performed using a diagnosis of overactive bladder as the dependent variable.

Covariates included TUGT score defined as fast, intermediate or slow, sex, age, race and number of medications. In order to explore a possible interaction between age and TUGT, a second model was created with interaction terms to this effect and models were compared using a likelihood ratio test. Analyses were performed using SAS 9.3 software.

Results

There were a total of 1363 individuals in our study with a TUGT, excluding 85 individuals in a wheelchair (15 with and 70 without an overactive bladder diagnosis) between December 2015 and July 2016. This number represents 76.5% of our total clinical population over the age of 65 during the period studied. This number includes individuals both with diagnoses of overactive bladder and those with other non-oncologic urologic diagnoses including upper and lower urinary tract stones, urinary retention, benign prostatic hyperplasia, erectile dysfunction, peyronie's disease, neurogenic bladder and male urethral stricture disease. Out of this number, there were 201 (14.8%) individuals identified with a diagnosis of overactive bladder. Individuals with overactive bladder were more likely to be female (52.2% compared to 18.9%, $p<0.0001$), slightly older (mean age 75.1 ± 7.1 compared to 72.9 ± 6.2, $p<0.0001$), have a slower mean TUGT time (13.7 ± 7.9 compared to 10.9 ± 5.2, $p<0.0001$) with 32.3% being classified as “slow” or “frail” compared 11.0% in the non-overactive bladder group ($p<0.0001$) and to have a greater number of office visits (2.3 ± 1.9 compared to 1.7 ± 1.1, $p<0.0001$) (Table 1).

Multivariable logistic regression was used to determine associations with a diagnosis of overactive bladder (Table 2). Overactive bladder was significantly associated with slow TUGT times (adjusted OR 3.0; 95% CI 2.0-4.8) and with being female (adjusted OR 4.4; 95% CI 3.2-6.1). Age, race and number of medications were not significantly associated with a diagnosis of overactive bladder.

We assessed potential interactions between age and the categorized TUGT variable by constructing a second logistic model that included TUGT by age interaction terms and tested the statistical significance of these interactions using a likelihood ratio test. The model was adjusted for sex, race and medication category. The p-value for the likelihood ratio test was 0.43, indicating that we could not detect statistically significant TUGT by age interactions and that our main effects only model was appropriate.

Comment

Patients with overactive bladder have statistically significantly slower TUGT times, which is closely associated with frailty, compared to patients seeking care for other non-oncologic urologic diagnoses among our clinical population. This finding holds true even after adjusting for other factors including age, sex, race, and number of medications, thereby suggesting that frailty, is common among and significantly associated with overactive bladder. Age, on the other hand, is not a statistically significant predictor of overactive bladder when adjusting for slower TUGT/frailty, sex, race and number of medications.

This is the first study to directly investigate and demonstrate a relationship between frailty and overactive bladder in the older population, strengthening the suggestion that frailty

should be considered in the workup and management of this condition due to its important clinical implications.[13] Our study demonstrates that individuals with OAB are less likely to have fast TUGT times (41.8% versus 60.8%) and are more likely to have slow TUGT times (32.3% versus to 11.0%) when compared to older individuals with other non-oncologic urologic diagnoses. While there are many ways to evaluate frailty in the clinical setting, we advocate for using the timed up and go test as a parsimonious and practical tool. Further investigation is needed in this area, however, the identification of frailty may be related to worse outcomes associated with certain overactive bladder treatment strategies and could potentially help to preferentially select optimal care strategies in these individuals. The identification of frailty could also serve as an impetus for referral to a geriatrician, nutritionist, physical therapist, or other specialist when appropriate.

Overactive bladder has been shown to be associated with urinary incontinence, specifically urgency or mixed urinary incontinence,[14-16] and is a topic of growing interest.[9] Among nursing home residents with urinary incontinence and/or overactive bladder, there is also a higher burden of moderate-to-severe cognitive impairment, severe mobility impairment, and comorbidities compared to residents without these conditions.[17] It has also been suggested that urinary incontinence may, in fact, be an early marker of frailty.[16]

Our overactive bladder population is not only frailer than our non-overactive bladder population but is also frailer compared to larger age-matched community dwelling populations. Others have reported that the mean TUGT among community-dwelling adults without disabilities is 8 seconds for men and women ages 60-69, 9 seconds for men and women ages 70-79 and 10 seconds for men and 11 seconds for women ages 80 to 89.[18] All of these numbers, regardless of age, are lower than the TUGT value of 13.7 seconds among our overactive bladder population. Others have estimated that 10% to 20% of community-dwelling individuals ages 65 and older are frail, depending on the definition of frailty and the population studied.[19,20] These values compare to our overactive bladder cohort where 25.9% were intermediately frail and 32.3% were frail based on the TUGT categorization.

The mechanistic underpinnings behind the relationship between frailty and overactive bladder remain unknown, but may be related to an increased incidence of cognitive decline, dementia, physical trouble getting to the bathroom in time, or possible changes to the bladder itself that have yet to be identified. The current paradigm attempts to explain the development of overactive bladder in terms of mechanistic changes related to aging. Functional magnetic resonance imaging (fMRI) and animal studies have demonstrated that there are several changes that occur in older individuals with overactive bladder including alterations in neural control of the bladder (heightened activation of the anterior cingulate cortex and the prefrontal cortex),[21] changes in the urothelium,[22] changes in muscarinic and purinergic neurotransmitters and receptors,[23] and inflammatory related changes to the bladder.[24]

However, the findings from our study introduce the concept that slower TUGT speed, or frailty (adjusted for age, race, sex and number of medications) is a statistically significant predictor for OAB, while age (adjusted for slow TUGT speed/frailty, race, sex and number of medications) is not, opening the possibility for an updated conceptual model that

incorporates frailty. Frailty is a complex and dynamic phenotypic state that represents a particular vulnerability to stressors and adverse events and results from cumulative declines across multiple organ systems that often lead to deterioration and adverse events.[25] The association between frailty and overactive bladder may not only be useful to consider in our treatment of individuals with overactive bladder, but may also be important to consider in evaluation of frail individuals, whereby it may be helpful to ask these individuals about their bladder, and specifically about overactive bladder symptoms.

The main limitation of our study is that our findings represent individuals from one academic urology setting, potentially introducing bias towards sicker or frailer individuals. However, our clinical population is likely comparable to other like academic practices. Further studies including other populations would be helpful to determine the generalizability of these findings. Another limitation is that we used a single measure of frailty, which has been shown in one study to have a sensitivity of 0.93 and a specificity of 0.62, meaning that there may be high false positive of frailty based on our definition.[26] We recognize that frailty is a dynamic and complex diagnosis that is distinct from both comorbidity and disability and that there is no one single measurement for frailty that is perfect. However, we feel that the TUGT is an ideal measure to use in the clinical setting based on its simplicity, ease of administration by medical staff, and demonstrated association with postoperative complications and increased 1-year mortality when studied among surgical patients.[12] Additionally, we recognize that our study may introduce a selection bias, whereby older individuals who have slower walking speeds on the TUGT take more time to get to the bathroom after perception of bladder urgency and may experience worse overactive bladder symptoms compared to their faster counterparts. We do recognize that the mobility aspect associated with overactive bladder is real, however, it is also representative of real-world patients who with these overlapping conditions and is therefore generalizable to the greater population.

Conclusions

Frailty, as measured by the TUGT, is strongly associated with a diagnosis of overactive bladder, even after adjusting for age, race, sex and number of medications among older individuals seeking care for non-oncologic urologic issues. This finding is significant in that it starts to shift our current understanding of overactive bladder from an age-related to a potentially age and frailty-related condition. Further investigation is required to better understand the relationship and mechanisms underlying this association.

Acknowledgments

Dr. Suskind's time was funded by NIDDK K12 DK83021-07; K12 Urologic Research (KURe) Career Development Program

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Table 1

Patient demographic and clinical characteristics

Characteristic	Total	OAB	Non-OAB	P value
Total N (%)	1363 (100.0)	201 (14.8)	1162 (82.3)	
Female N (%)	324 (23.8)	105 (52.2)	219 (18.9)	<0.0001
Age (Mean ± SD)	73.3 ± 6.4	75.1 ± 7.1	72.9 ± 6.2	<0.0001
Age Group N (%)				
65-70	560 (41.1)	62 (30.9)	498 (42.9)	0.0028
71-75	386 (28.3)	57 (28.4)	329 (28.3)	
76-80	217 (15.9)	43 (21.4)	174 (15.0)	
81 +	200 (14.7)	39 (19.4)	161 (13.9)	
Race N (%)				
White	887 (65.1)	130 (64.7)	757 (65.2)	0.2037
Black	56 (4.1)	5 (2.5)	51 (4.4)	
Asian	166 (12.2)	32 (15.9)	134 (11.5)	
Others	254 (18.6)	34 (16.9)	220 (18.9)	
Urinary incontinence	166 (12.3)	77 (38.3)	91 (7.8)	<0.0001
Number of medications (Mean ± SD)	14.2 ± 8.4	16.5 ± 8.4	13.8 ± 8.3	<0.0001
Medication categories				
1-5	178 (13.1)	15 (7.5)	163 (14.0)	0.0006
6-10	343 (25.2)	39 (19.4)	304 (26.2)	
11-15	340 (24.9)	47 (23.4)	293 (25.2)	
16-20	224 (16.4)	45 (22.4)	179 (15.4)	
>20	278 (20.4)	55 (27.4)	223 (19.2)	
TUGT (Mean ± SD)	11.3 ± 5.8	13.7 ± 7.9	10.9 ± 5.2	<0.0001
TUGT Group N (%)				
Fast (≤ 10 sec)	790 (58.0)	84 (41.8)	706 (60.8)	<0.0001
Intermediate (11 to 14 sec)	380 (27.9)	52 (25.9)	328 (28.2)	
Slow (≥ 15 sec)	193 (14.2)	65 (32.3)	128 (11.0)	
Number of office visits in time period (Mean ± SD)	1.8 ± 1.3	2.3 ± 1.9	1.7 ± 1.1	<0.0001

Table 2

Regression model predicting a diagnosis of overactive bladder.

Characteristic	OR & 95% CI	P value
Sex		
Male	Ref.	
Female	4.4 (3.2 – 6.1)	<0.0001
Age Group		
65-70	Ref.	
71-75	1.2 (0.8 - 1.9)8 – 2.0)	0.3304
76-80	1.6 (1.0 - 2.5)	0.0689
81 +	1.4 (0.8 - 2.3)	0.2374
Race		
White	Ref.	
Black	0.4 (0.2 - 1.1)	0.0883
Asian	0.9 (0.6 - 1.5)	0.7937
Other	0.9 (0.6 - 1.4)	0.6978
Medication categories		
1-5	Ref.	
6-10	1.1 (0.6 - 2.2)	0.6851
11-15	1.3 (0.7 - 2.5)	0.4179
16-20	1.9 (1.0 - 3.6)	0.0672
>20	1.4 (0.7 - 2.7)	0.3242
TUGT		
Fast (≤ 10 sec)	Ref.	
Intermediate (11 to 14 sec)	1.1 (0.8 - 1.7)	0.5841
Slow (≥ 15 sec)	3.0 (2.0 - 4.8)	<0.0001